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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,078	02/16/2000	Manuel Campos	PC10202A	5616

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EXAMINER	
FOLEY, SHANON A	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/506,078	Applicant(s) CAMPOS ET AL.	
	Examiner Shanon Foley	Art Unit 1648	

-- Th MAILING DATE of this communication appears on th cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Drawings

Applicant has satisfactorily amended the specification to include a complete brief description for each drawing originally submitted. Drawing corrections and/or the substitute sheets of drawings that were indicated in the Notice of Draftspersons Patent Drawing Review is held in abeyance until the case is deemed allowable.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 11, 13, and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant states that the language in question, recited in independent claims 1 and 3 is "a first proteinaceous portion analogous to all or part of an endogenously synthesized protein within a vertebrate." Applicant asserts that the language is being read in vacuum and is not indefinite when the claims are read as a whole and is further defined by three limitations set forth in the independent claims and the specification. The first is that the peptide is endogenously synthesized, the second is that the protein activity is inhibited as a results of an immune response directed against the protein, and the third is that the protein is incapable of eliciting an immunoinhibitory immune response in the host. Applicant asserts that it would be well understood by in the art what an endogenously synthesized protein would be and that whether these proteins are vital is a moot point.

Applicant's arguments have been considered, but are found unpersuasive. While it is conceded that there are many peptides known to be expressed in a host and that some of these proteins are used to inhibit or diminish protein function once administered, the scope of the claims encompass all endogenous peptides and is indefinite. The structure and/or function of every endogenously made peptide in a host are not known. Therefore, claims encompass peptides with no known structure or function. Due to the lack of knowledge regarding unknown and undiscovered peptides, it cannot be asserted that every endogenously made peptide would be capable of eliciting an immunoinhibitory immune response in the host or whose activity would be inhibited as a results of an immune response directed against the protein. The specification does not structurally or functionally define all endogenously made peptides and does not teach that all peptides expressed in a host are capable of the required functions in the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 11, 13, and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a fusion protein that inhibits the function in the class of gonadotropins and BHV, does not reasonably provide enablement for a fusion protein that inhibits the function of any endogenously made protein and protects against any disease in a vertebrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. This rejection is maintained for reasons of record.

Applicant asserts that the claims are being interpreted beyond the words of the claims. Applicant also states that examples of proteinaceous portions that are analogous to all or part of a peptide is well known in the art and the Office has not submitted any references indicating that these proteins are not well known in the art. Applicant argues that a list of all endogenously made proteins would be exhaustive and that even if such a list were compiled, the skilled artisan would know what the peptides are anyway. Applicant contends that if the Office views all endogenously made peptides and any proteinaceous portions of any immunogen of any pathogen not well known in the art, the Office is to refuting all microbiology and immunology texts in existence. Applicant concludes that the Office does not provide a basis for the enablement rejection in fact or law.

Applicant's arguments and assertions have been fully considered, but are found unpersuasive. The first factor to be considered for establishing undue experimentation is the breadth of the claims, see the MPEP § 2164.01 (a) and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The scope of the instant claims encompasses inhibiting the function of every known or unknown protein made in a vertebrate while protecting against every disease that may be encountered by the vertebrate by administering the instant fusion protein. This scope of the claims is derived from the actual words recited in the claims, which encompass every known and unknown protein endogenously made in a vertebrate and protecting against every disease that may be encountered by the host by administering a proteinaceous analogous to any immunogen of any known or unknown pathogen. It is conceded that the proteins cited in the art are known to some degree, some much more so than others. However, there is no indication in the prior art or in the instant specification that every possible protein

internally manufactured by a vertebrate and every possible immunogen from every unknown and known pathogen have been discovered and structurally and functionally defined. The second factor for determining undue experimentation is the nature of the invention, which is drawn to eliciting a dual immune response of inhibiting the function of any endogenously synthesized protein and protecting against any pathogen encountered by a vertebrate by administering the instant fusion protein. The specification has not described the structure or function for all of the proteins made in a vertebrate, or what result of inhibiting the function of any protein would do to the vertebrate when administered (except for GnRH). Nor does the specification demonstrate that incorporating any protein from any pathogen into the claimed fusion protein protects against every pathogen. This lack of information lends itself to a lack of ability for one skilled in the art to structurally and functionally identify all possible endogenous peptides and immunogens from pathogens and a lack of predictability for whether the instant fusion protein would perform the required functions in recited in the claims. This level of skill for one skilled in the art and the lack of predictability in the art are the fourth and fifth elements to be considered for determining undue experimentation. The MPEP § 2164.01 (b) states that a key issue for determining lack of enablement is whether the starting materials are available. In the instant case, all of the starting materials that are unknown in the art, i.e. yet-to-be discovered pathogens and every endogenously synthesized peptide are not available. Therefore, the skilled artisan is unable to make or use these proteins. The sixth and seventh factors for determining lack of enablement in the MPEP § 2164.01(a) are the amount of direction provided by the inventor and the existence of a working example. The examples on page 34-43 are limited to the fusion protein gD/GnRH and the specification provides no teaching for that would enable the skilled artisan to identify every

endogenous vertebrate peptide and fuse it to every immunogen of any known or unknown pathogen. In conclusion, the Office has identified what information is missing and why the skilled artisan would not be able to bridge the gap between what is known and what is needed to practice the invention without undue experimentation in accordance with the case law and the MPEP. In response to the lack of references cited to support the lack of enablement rejection, supporting references are not required, see *In re Marzocchi*, 439 F.2d 220, 224, 169, USPQ 367, 370 (CCPA 1971). Therefore, the Office has met its burden of establishing a prima facie obvious case of lack of enablement to practice the invention in its full scope.

Claim Rejections - 35 USC § 103

The following is a quotation of 35.U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Der Zee et al. (5,684,145) and Mittal et al. for reasons of record.

Applicant admits that the Van der Zee et al. reference teaches a carrier system to vaccinate mammals against GnRH and that the hormone is not immunogenic and must be administered with an immunogenic carrier to activate an immune response against GnRH. Applicant also agrees that the reference does not teach producing a dual immune response using GnRH in a fusion protein. Applicant also agrees that Mittal et al. teaches an adenovirus which expresses the gD protein of BHV-1 and that gD is antigenic on its own. Applicant also agrees with *In re Fine* cited by the Office, but contends that the issue is not whether the combination of

references is obvious to the Office, but whether it would be obvious to one of ordinary skill in the art and the only way to prove this would be gleaned from the references themselves.

Applicant states that the prior art must at least describe a fusion protein that induces a dual immune response and that there is absolutely no motivation to combine these references without such a teaching. Specifically, applicant argues that the references only evoke a single immune response. Van der Zee et al. emphasizes that GnRH be located at a specific cite that is critical for immunogenicity and the motivation of Mittal et al. is drawn to lowering the cost of vaccine production. Applicant argues that a dual immune response elicited by combining the two peptides in the instant fusion protein is a surprising result in the art in light of the criticalities discussed in the prior art cited.

Applicant's arguments as well as a review of the references have been fully considered, but are found to be unpersuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the test of obviousness is not an express suggestion of the claimed invention in any or all references but <u>what references taken together would suggest to those of ordinary skill in the art</u> presumed to be familiar with them (emphasis added).

Applicant has argued that the cited prior art does not describe a fusion protein that induces a dual immune response. Claim 1 of Van der Zee et al. is drawn to a recombinant DNA

molecule that encodes a hybrid protein. This hybrid protein contains two portions derived from two distinct and unrelated proteins: an *E. coli* P-fimbrial major subunit and an antigenic determinant of GnRH. Therefore, the hybrid protein of Van der Zee et al. is a fusion protein. Although Van der Zee et al. does not teach a specific immune response directed against the *E. coli* P-fimbrial major subunit portion of the subunit protein, the reference does teach that the *E. coli* P-fimbrial subunit is a strong immunogenic carrier which possesses strong antigenic characteristics that is required to induce an immune response against GnRH, see column 4 of Van Der Zee et al. Therefore, although Van der Zee et al. does not specifically teach the immune response directed against the P-fimbrial subunit, the natural antigenic properties possessed by the protein filaments would induce an immune response. This immune response is evidenced by the specific potentiation directed against GnRH in the hybrid protein containing the *E. coli* P-fimbrial major subunit. Therefore, Van der Zee et al. teaches a fusion protein comprising GnRH that induces a dual immune response. Van Der Zee et al. do not include using gD from BHV-1 as the immunogenic component to the fusion protein.

However, Mittal et al. teaches that a full-length recombinant form (gD) from BHV-1 inserted into a human adenovirus type 5 vector. It is well established in the art that gD is highly antigenic on its own.

One of ordinary skill in the art at the time the invention was made would have been motivated to substitute the strong immunogenicity of BHV-1 gD taught by Mittal et al. with the *E. coli* P-fimbrial subunit portion of the hybrid protein of Van Der Zee et al. to evoke an immune response against GnRH and protect against BHV-1. One of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention because the

teachings of Van Der Zee et al. indicate that all that is needed to induce an immune response against GnRH is a strong immunogenic carrier, which is what gD from BHV-1 is. Further, it is conventional practice in the vaccine arts to incorporate highly antigenic glycoproteins into a vaccine; therefore, one of ordinary skill in the art would view the incorporation of gD into the hybrid protein taught by Van Der Zee as an obvious substitution over the *E. coli* fimbrial-filiments. Therefore, it is maintained that the instant invention would have been pima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence to evidence to the contrary.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley/SAF
June 22, 2002

James C. Housel 7/1/02

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